Remarks

Claims 1-117 are canceled herein. Applicants reserve the right to pursue the subject matter of claims 1-117 in continuing applications. New claims 118-135 are added herein and are pending in the application.

Support for claim 118 can be found, *inter alia*, at paragraphs 22-25, beginning on page 4 of the specification. Support for claim 119 can be found, *inter alia*, at paragraph 280 on page 109. Support for claims 122, 123 and 125 can be found, *inter alia*, at paragraph 46, page 10 of the specification. Support for claim 124 can be found, *inter alia*, at paragraph 210, page 63 of the specification. Support for the remaining new claims can be found, *inter alia*, in the originaly filed claims as outlined in the table below.

New Claim	Original Claim
120	69
121	66
126	64
127	68
128	74
129	75
130	76
131	77
132	78
133	79
134	80
135	82

I. Specification

The Examiner has objected to the specification because of an error in the numbering of the pages. (Office Action, page 2.) Applicants thank the Examiner for pointing out this error. Filed with this reply is a substitute specification with corrected page numbering. The only changes in the substitute specification are to the page numbers, therefore there is no new matter.

II. Information Disclosure Statement

The Examiner noted an error in the citation of reference 192 of the information disclosure statement filed on December 5, 2005. Applicants thank the Examiner for pointing out this error. A supplemental information disclosure statement listing the correct reference is submitted with this reply.

III. Rejection of the Claims Under 35 U.S.C. § 112, First Paragraph

Claims 61-90, stand rejected under 35 U.S.C. § 112, First Paragraph, for failing to comply with the written description requirement. (Office Action, page 3.) Applicants respectfully disagree but have canceled claims and added new claims to facilitate prosecution.

The Examiner asserts that the claims do not recite a nexus between any treatment and any element of the nucleic acid complex, such as a fluorophore or any functional relationship between any treatment and a specific element of the complex. (Office Action, page 3.) New claim 118 is submitted herein and recites contacting the cell "with light having a wavelength absorbed by the fluorescent molecule such that the nucleic acid molecule is disassociated from the complex." Applicants believe that new claim 118 addresses the Examiner's concerns and meets the requirements of 35 U.S.C. § 112, First Paragraph.

The Examiner asserts that the metes and bounds of claims 73, 83 and 84 cannot be known because the herpes simplex virus is subject to mutation. (Office Action, page 4.) Claims 73, 83 and 84 have been canceled herein rendering this rejection moot.

In view of these amendments and remarks, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, First Paragraph.

IV. Rejection of the Claims Under 35 U.S.C. § 102(b)

Claims 61, 63-75, 80-90 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Curiel *et al.* (U.S. Patent No. 5,547,932). (Office Action, page 5.) Applicants respectfully disagree.

In order to anticipate, a single reference must disclose "each and every limitation of the claimed invention." (*Helifix Ltd. v. Blok-Lok, Ltd.*, 208, F.3d 1339, 1346 (Fed. Cir. 2000).) The Examiner asserts that the transferrin molecule used in the methods taught by Curiel *et al.* is a fluorescent molecule because it comprises "many aromatic amino acids." (Office Action, page 5.) Curiel *et al.* does not teach "contacting the cell with light having a wavelength absorbed by the fluorescent molecule such that the nucleic acid molecule is disassociated from the complex." Thus, because Curiel *et al.* does not teach the use of light as in the present invention as claimed, Curiel *et al.* does not anticipate.

Claims 61-68, 70-75, 80, and 83-90 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Normand *et al.* (*J.Biol. Chem. 276*:15042-15050 (2001)) in view of GenBank Accession No. BAE87004, 3/17/06 and http://www.clinalfa.com/docs/docs/PROT/TB070.pdf. (Office Action, page 6.) Applicants respectfully disagree.

The Examiner asserts that Normand *et al.* discloses methods of delivering to cells a complex of a VP22 fusion protein and fluorescein labeled antisense oligonucleotides, and illuminating the cells with light in order to dissociate the oligonucleotides from the fusion protein. (Office Action, page 6.) New claim 118 recites "wherein the nucleic acid molecule is not covalently bound to the fluorescent molecule." The fluorescent molecules of Normand *et al.*, as described in the experimental methods section, are covalently attached to the nucleic acids, therefore Normand *et al.* does not anticipate claim 118.

Claims 61-75 and 80-90 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Berg *et al.* (U.S. Patent Application No. 2002/0155099). (Office Action, page 7.) Applicants respectfully disagree.

Berg *et al.* discloses a method for releasing molecules into the cytosol of cells by allowing the molecules to be taken up into endosomes and treating the cells with a photosensitizer that localizes to the endosomes and exposing the cells to light resulting in release of the molecule from the endosome into the cytosol. Berg *et al.* distinguishes between photosensitizers and the fluorescent compounds of the present invention in Example 13. In this example, fluorescein was used as a label for the ribozyme and the photosensitizer $AlPcS_{2a}$ along with light was used to disrupt the endosomal membrane. If fluorescein was a suitable compound for the invention of Berg *et al.*, the addition of

$A1PcS_{2a}$ would not have been necessary. Further, the photosensitizers of Berg *et al.* as described in paragraph 50, on page 4 including compounds such as prophyrin, phtalocyanine, purpurin are not the same as the fluorescent compounds described in the present specification at paragraph 283, on page 110 through paragraph 295, page112 which include compounds such as eosin, fluorescamine, fluorescein and rhodamine derivatives etc. One of ordinary skill in the art, on reading Example 13 of Berg *et al.* and the present disclosure, would understand that the photosensizers of Berg *et al.* are not fluorescent molecules as the term is used in the present claims. Because the flouorescent molecules of the present invention do not act to disrupt endosomal membranes as disclosed by Berg *et al.*, Berg *et al.* does not anticipate the present invention.

In view of the above, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of the claims under 35 U.S.C. § 102(b).

IV. Rejection of the Claims Under 35 U.S.C. § 103

Claims 61, 71 and 74-79 stand rejected under 35 U.S.C. as being unpatentable over Wahl *et al.* (U.S. Patent No. 5,654,182) in view of either Curiel *et al.* or Berg *et al.* (Office Action, page 9.) Applicants respectfully disagree but have canceled claims and added new claims to facilitate prosecution.

Wahl *et al.* discloses methods for integrating nucleic acids into the genome of a cell using recombination mediated by an FLP recombinase. Wahl *et al.* does not teach or suggest the use of fluorescent molecules, cellular delivery proteins or "contacting the cell with light having a wavelength absorbed by the fluorescent molecule such that the nucleic acid molecule is disassociated from the complex." The Examiner asserts that one skilled in the art would be motivated to use the methods of Curiel *et al.* or Berg *et al.* to facilitate the integration of nucleic acids into the genome of a cell as taught by Wahl *et al.*

"A patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. (See *KSR Int'l v. Teleflex Inc.,* U.S. 2007 (2007 WL 1237837 (U.S.).) The Examiner asserts that a recombinase in Wahl *et al.* may be considered a cellular delivery polypeptide because they catalyze the delivery of nucleic acids into the genome. (Office Action, page 10.) However, cellular delivery molecules are defined in the present specification at paragraph 23, page 4

as molecules which facilitate translocation into a cell, not into a genome. Therefore one of ordinary skill in the art would not look to Curiel *et al.* to arrive at the present invention because different reagents are required. Applicants assert that one of ordinary skill in the art would not look to Berg *et al.* because, as discussed above, the photosensitizer compounds of Berg *et al.* are not the same as the fluorescent compounds claimed in the present invention. In view of the foregoing, Applicants respectfully assert that the Examiner has not established a *prima facie* case of obviousness.

In view of the above, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of the claims under 35 U.S.C. § 103.

Conclusion

Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Reply is respectfully requested.

Respectfully submitted,

/Peter G. Foiles/

Peter G. Foiles
Agent for Applicants
(240) 379-4173
Registration No. 46,477

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